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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/981,460	10/16/2001	Daniel S. Kohane	0492611-0418 (MIT 9023)	5906

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EXAMINER	
BURKHART, MICHAEL D	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 02/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/981,460	KOHANE ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 1/13/2006.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1, 2, 7-48, 51, 53, 54, 57-63, 65-79 is/are pending in the application.

4a) Of the above claim(s) 25,28,34-36 and 41-44 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,2,7-24,26,27,29-33,37-40,45-48,51,53,54,57-63 and 65-79 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/15/2005 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 7-24, 26, 27, 29, 30-33, 37-40, 45-48, 51, 53, 54, 57-63, and 65-79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2, 63, 69 and 73 recite microparticles that comprises 3-99% by weight lipid, 1-60% by weight protein, and 0.5-50% by weight sugar. It is unclear how a microparticle comprising the upper limit of the lipid range (99%) could also comprise both of the other two recited components, which would render a particle with a total of weight/weight ratio of 100.5% (i.e, 99% lipid, 1% protein and 0.5% sugar). Therefore, the metes and bounds of the claimed subject matter are unclear.

Claims 1, 2, 63, 69 and 73 recite microparticles prepared by "spray drying, single and double emulsion solvent evaporation, solvent extraction, phase separation, and simple and

complex coacervation". It is unclear if these are method steps to be used in conjuction to arrive at the claimed microparticles, or if they are separate methods that each might produce the claimed microparticles. If the former, it would be remedial to clearly define any distinct method steps of the claims, or, if the latter, to claim the different methods using proper Markush language (i.e. selected from the group consisting of:). This rejection affects all dependent claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 7-17, 20-24, 26, 27, 29-33, 37-38, 40, 45-47, 51, 53, 54, 57-62, 65-70, 73-74, and 77-79 are rejected under 35 U.S.C. 102(b) as anticipated by Sutton (US 6,204,054) or, in the alternative, under 35 U.S.C. 103(a) as obvious over 6,204,054. This rejection is maintained for reasons made of record in previous Office Actions (Non-Final Rejection of 6/15/04 and Final Rejection of 1/11/2005) and for reasons set forth below.

Response to Arguments

Applicant's arguments filed 6/15/2005 have been fully considered but they are not persuasive. Applicants argue that: 1) Sutton does not teach microparticles with at least three components in the matrix of the microparticles, as found in the instant claims; 2) Sutton does not specifically teach the weight ranges of the instant claims, the use of lactose, or the use of DPPC, albumin and lactose.

Regarding 1) and 2), the use of all three components in the microparticles by Sutton was clearly described on page 7 of the Final Rejection (1/11/2005), which included albumin, lactose, and DPPC. The Sutton reference as a whole particularly teaches that any combination of biocompatible materials, excipients, emulsifiers, and/or pharmaceutical acceptable excipients can be incorporated into albumin based vesicles and/or enhancers, wherein all of the excipients/protector/albumin form microcapsules comprising a physiologically active agent conjugated to albumin or embedded in the microparticles. The combinations of these components and additional excipients, stabilizers, flavoring substances, carriers, etc. are used to incorporate various components and/or combinations for optimization, and are considered to be

well-established in the prior art, see column 9-10. As such, to the extent that the instant claims embrace various minor modifications including those of design choice, *e.g.*, diameter, weight percentage of each of the components, DNA derivatives, modified sugars and/or modified lipids, such would have been obvious to one of ordinary skill in the art. A close review of the as-filed specification show that no unexpected results arise from any of these claimed combinations, and that components varying in weight percentage and/or components such as derivatized lipids are employed interchangeably in the prior art. Thus, it is obvious to substitute for one another components that are known in the prior art to have equivalent characteristics in the claimed compositions. Likewise, the microparticles of Sutton would then be suitable to encapsulate and/or deliver any drug of choice such as DNA, RNA or plasmid coding for a protein or antigen of interest. As such, it would also have been obvious for one of ordinary skill in the art of polymer or microparticle to employ any combination of ratio or percent weight of each of the biocompatible material as a matter of design choice for the making of claimed composition, particularly since the reference clearly teaches that as long as albumin is employed, combinations of albumin, sugar, lipids and/or other excipients/stabilizers can be formulated to make a claimed vesicle or microparticle designed for use as a carrier of any biologically active molecules such as antigen encoding DNA, plasmids, expression vectors, and recombinant DNA(s).
Notwithstanding the reasoning for rendering the claimed invention as broadly claimed anticipated by Sutton, there clearly exist general art accepted motivations for formulating an excipient such as a protein, a sugar and/or a lipid such as DPPC into the albumin based polymer of Sutton, that is to modify the dispersibility, rate of biodegradability, elasticity and water permeability (pages 13-14 of the Final Rejection, taken from Sutton). These general art accepted

motivations are valid because of an absence of valid evidence showing unexpected results commensurate with the full breadth of the claimed invention.

Thus, the Sutton reference anticipates, or in the alternative, renders the claimed invention as a whole *prima facie* obvious.

Claims 1, 18, 19, and 73-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sutton (as above) taken with Grinstaff (5,639,473).

Claims 69, 71, and 72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sutton (as above) taken with Grinstaff (5,639,473).

Claims 1, 2, 7-24, 26, 27, 29-31, 33, 37-40, 45-48, 51, 53, 54, 57-63, 65-69 and 73-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hanes (5,855,913).

Claims 1, 2, 7-24, 26, 27, 29-31, 33, 37-40, 45-48, 51, 53, 54, 57-63, 65-69 and 73-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hanes (5,855,913).

Claims 1, 2, 7-24, 26, 27, 29-33, 37-40, 45-48, 51, 53, 54, 57-63, 65-69, and 73-79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hanes taken with any of Grinstaff, Sutton, or Rypacek (GB 2174097 A), and further in view of Wheeler (5,976,567).

These rejections are maintained for reasons made of record in previous Office Actions (Non-Final Rejection of 6/15/04 and Final Rejection of 1/11/2005) and for reasons set forth below.

Response to Arguments

Applicant's arguments filed 6/15/2005 have been fully considered but they are not persuasive. Applicant's arguments for the above 103(a) rejections are essentially the same, and

present many of the same arguments as addressed above in the Sutton 102/103 rejection. Applicants argue that: 1) neither Grinstaff, Wheeler, nor Hanes teaches microparticles with at least three components in the matrix of the microparticles, as found in the lipid-protein-sugar matrix of the instant claims; 2) neither the Sutton and Grinstaff combination, the Sutton and Wheeler combination, nor Hanes specifically teaches the weight ranges of the instant claims.

Regarding 1) and 2), see the response above for the Sutton 102/103 rejection. Additionally, Hanes suggests that any combination of biocompatible materials such as therapeutic agents, polymers, lipid surfactants and protein/sugar excipients can be used to make the encapsulated particles so that the particles are basically formulated to become polymeric microparticles for drug delivery to the pulmonary system, wherein the particles having an appropriate size such as at least 5 microns in diameter, and wherein the polymeric particles are capable of biodegrading at a controlled rate for delivery of a drug (see column 5, last full par.), and column 7 through column 8. The particular use of DPPC (lipid), protein, and a sugar by Hanes are pointed out on pages 20-23 of the Final Rejection (1/11/2005). Clearly, Hanes recognizes the desirability of incorporating excipients and/or targeting agents into the DPPC/blended protein based polymer for improving and/or optimizing degradation rates and release times (page 26 of the Final Rejection, 1/11/2005), thus providing further motivation, in addition to that recited by Sutton above, for the incorporation of three or more of the disclosed components into the matrix.

Conclusion

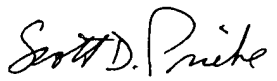
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael D. Burkhart
Examiner
Art Unit 1633



SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER